REMARKS

Claims 1-33 are pending in the application. Claims 1, 2-6, 8-10 and 12-14 are allowed. Claims 7, 11, and 15-33 have been rejected.

Claim 2 has been amended to provide antecedent basis for the term antigen.

Claims 7, 11 and 15-33 have been rejected under 35 U.S.C. §103(a) as allegedly unpatentable over Tice ('330). Applicants respectfully traverse this rejection.

Claims 7 and 11 are dependant on allowed claims. If the base claims upon which these claims are dependant have been deemed by the Examiner to be allowable, Applicants submit that claims 7 and 11 are also allowable because they further limit the allowed base claims; even withstanding the use of the term "consisting of." The rejection of claims 7 and 11 should be withdrawn.

Claims 15-33 are drawn to an immunostimulating composition that comprises encapsulating microspheres of poly(lactid/glycolide) as a bulk matrix and an immunogenic substance comprising a "conformationally native subunit of chronic intracellular pathogen which in the course of natural infection with that pathogen, is exposed to the host immune system on the surface of free pathogen and/or pathogen-infected cells." The term "conformationally native subunit" is not suggested in Tice '330.

A conformationally native subunit is described in column 2, lines 3-9 of the present specification. The inventors endeavored to solve the problems of the past. In the past, especially in the case of HIV-1 infection, there was insufficient information available to make a preventative vaccine. Many candidate HIV vaccines tested failed to elicit antibodies capable of neutralizing wild-type HIV-1 or binding to native HIV-1

proteins and also failed to induce a substantial population of effector cells capable of destroying HIV-1 infected cells or inducing significant responses at mucosal surfaces. The inventors have solved this problem for HIV-1 and other chronic intracellular pathogens by identifying a native subunit, accessible to the immune system on the surface of both free virus and infected cells and presenting it to the immune system (systemically and mucosally) encapsulated in a microsphere to protect and augment its immunogenicity. (claim language underlined).

Tice '330 does not teach this novel feature. Although Tice discusses antigens as possible candidates for microencapsulation, Tice does not disclose the employment of conformationally native subunits, accessible to the immune system on the surface of both free virus and infected cells.

The term "antigen" used by Tice is a very broad term. A conformationally native subunit is a small part of an antigen and is part of a pilus protein.

In addition to being very immunogenic for the intended purpose, a conformationally native subunit is very difficult to encapsulate because of its delicate nature. The inventors have successfully encapsulated this very delicate molecule PLGA microspheres without destroying it. One of ordinary skill in the art would have recognized that such a delicate molecule as is presented in the claims is easily destroyed in the encapsulation process because it is subjected to solvents and temperatures that can ruin its effectiveness as an immunogenic substance. Tice does not provide any teaching of how to encapsulate a conformationally native subunit and one of ordinary skill in the art would have required undue experimentation to solve the problem. As previously

stated, previous vaccines failed to elicit antibodies capable of neutralizing infection or binding to native proteins and being effective.

Further, the highlighted excerpts of Tice '330 indicate the encapsulation of progesterone and norgestimate. These are hormones rather than conformationally native subunits as claimed and described. These hormones would not have lead one of ordinary skill in the art to the claimed invention.

In light of this explanation, it is submitted that one of ordinary skill in the art would not have been motivated by the disclosure of Tice '330 to encapsulate "conformationally native subunit of chronic intracellular pathogen which in the course of natural infection with that pathogen, is exposed to the host immune system on the surface of free pathogen and/or pathogen-infected cells." The mere recitation of an antigen does not provide the necessary teaching to solve the problem that the inventors have solved, i.e. making an immunostimulating composition that is more immunogenic and that is presented in the form of a microsphere wherein the active ingredient (conformationally native subunit) is not destroyed in the encapsulation process. Hence the rejection under 35 U.S.C. §103(a) is believed overcome.

Reconsideration and allowance are respectfully requested.

Respectfully submitted,

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Versions with markings:

Please amend claim 2 as follows:

2. (Amended) The immunostimulating composition described in claim 1 wherein the immunogenic substance is an antigen and the antigen is pre-encapsulated into a conformationally stabilizing hydrophilic matrix consisting of an appropriate mono, di- or tri-saccharide or other carbohydrate [susbstance] substance by lyophilization prior to its final encapsulation into the PLGA microsphere by a solvent extraction process employing acetonitrile as the polymer solvent, mineral oil as the emulsion's external phase, and heptane as the extractant.